1014. *2-Amino-2-imidazolines and 2-Amino-2-oxazolines.*

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2-Amino-2-imidazoline has been prepared by the cyclisation of 2-guanidinoethylamine, which is produced in poor yield by the action of ethylenediamine on *S*-methylisothiouronium sulphate. A better general method for the preparation of 2-amino-2-imidazolines and 1,4,5,6-tetrahydropyrimidines is the action of cyanamide or dimethylcyanamide on the monotoluene-*p*-sulphonates of 1,2- or 1,3-diamines. The action of phenylcyanamide gives the 2-anilino-derivatives. Ethylenediamine with 2-amino-2-imidazoline gives a mixture of *N*-2-imidazolinyl- and *NN'*-di-2-imidazolinyl-ethylenediamine rather than the bicyclic 2,3,5,6-tetrahydro-1*H*-imidaz[1,2*a*]imidazole previously reported. 2-(Substituted amino)-2-oxazolines have been prepared from *N*-substituted *N'*-2-hydroxyethylthioureas by the action of methyl iodide and sodium ethoxide, and by thermal cyclisation of *NN'*-diphenylguanidinoethanols, which are prepared from diphenylcarbodi-imide and amino-alcohols.

2-Amino-2-imidazoline has been obtained as its salt by the action of cyanogen bromide on ethylenediamine,[1] and its substituted derivatives have been obtained by the action of

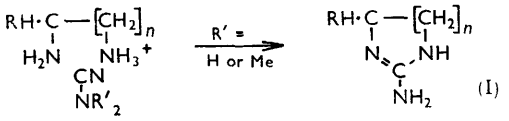
[1] Pierron, *Ann. Chim. Phys.*, 1919, **11**, 361.

amino-compounds on bromoethylcyanamides [2] or 2-methylthioimidazolines [3] or 2-nitroiminoimidazolidines.[4]

A possible synthetic route to 2-aminoimidazoline would be by ring closure of 2-guanidinoethylamine by loss of ammonia. This substance could not be obtained in appreciable quantity from cyanamide and ethylenediamine under various conditions, ethylenediguanidine being formed almost exclusively. A small yield of 2-aminoimidazoline, isolated as its picrate, was however obtained when the diamine reacted with methylisothiouronium sulphate at pH 7 and the intermediate monoguanidine sulphate was passed through Amberlite IRA-400 resin which effected ring closure.

A much better method of obtaining 2-aminoimidazolines was based on the procedure used for 2-substituted imidazolines by Oxley and Short [5] who heated cyanides with the monotoluene-*p*-sulphonate of ethylenediamine. This reaction has now been extended to include the use of cyanamide and substituted cyanamides.

When equimolecular amounts of ethylenediamine monotoluene-*p*-sulphonate and cyanamide are heated in the steam bath, ammonia is evolved and both ethylenediguanidine and 2-aminoimidazoline (I; R = H, n = 1) are formed as the toluene-*p*-sulphonates in about 20% yield. Use of dimethylcyanamide leads to dimethylamine formation and the



(I)

2-aminoimidazoline salt is readily isolated in about 50% yield. Either cyanamide or dimethylcyanamide (1 mol.) and trimethylenediamine (as monotoluene-*p*-sulphonate) similarly gave 2-amino-1,4,5,6-tetrahydropyrimidine (I; R = H, n = 2).

Benzimidazoles are readily formed from cyanamides and *o*-phenylenediamine, but, in the case of dimethylcyanamide, ammonia and not dimethylamine is evolved, the product being 2-dimethylaminobenzimidazole as confirmed by its preparation from 2-chlorobenzimidazole and dimethylamine.[6]

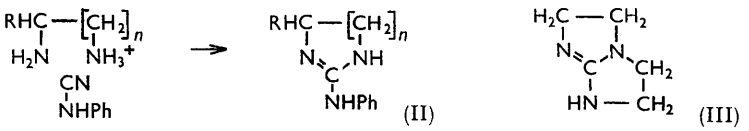
When phenylcyanamide reacts with ethylenediamine toluene-*p*-sulphonate, ammonia is slowly evolved, and from the product, consisting of both the diguanidino-derivative of ethylenediamine and the imidazoline, the latter can be isolated as picrate from which the free base is liberated. That this product is 2-anilino-2-imidazoline (II; R = H, n = 1) and not the 1-phenyl isomer, is proved by its preparation from 2-methylthioimidazoline by a modification of Aspinall and Bianco's method.[3] In the reaction between phenylcyanamide and trimethylenediamine toluene-*p*-sulphonate the corresponding 2-anilinotetrahydropyrimidine (II; R = H, n = 2) is produced.

Similar results were obtained with propylenediamine. With an equimolecular quantity of cyanamide or, better, with 2 mol. of dimethylcyanamide the toluene-*p*-sulphonate of 2-amino-4-methylimidazoline (I; R = Me, n = 1) is formed; the oily base gives a crystalline picrate and nitrate. When phenylcyanamide is used, the non-crystalline reaction product, after conversion into the picrate, yields the crystalline 4-methyl-2-anilinoimidazoline (II; R = Me, n = 1).

Pierron claimed [1] to have prepared the bicyclic 2,3,5,6-tetrahydro-1*H*-imidaz[1,2*a*]-imidazole (III) by heating 2-aminoimidazoline with an excess of ethylenediamine for 48 hr. He described a dipicrate, m. p. 203°, and a dihydrobromide, m. p. 224°. The product

[2] Elderfield and Hageman, *J. Org. Chem.*, 1949, **14**, 605; Elderfield and Green, *ibid.*, 1952, **17**, 442.
[3] Aspinall and Bianco, *J. Amer. Chem. Soc.*, 1951, **73**, 602; McKay and Hatton, *ibid.*, 1 56, **78**, 1618.
[4] McKay, Buchanan, and Grant, *J. Amer. Chem. Soc.*, 1949, **71**, 766.
[5] Oxley and Short, *J.*, 1947, 497.
[6] Efros, Porai-Koshits, and Farbenshtein, *Zhur. obshchei Khim.*, 1953, **23**, 1691.

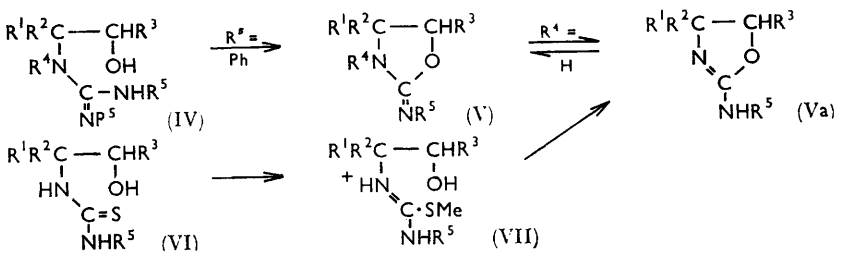
obtained by us under his conditions was converted into the picrate; fractional crystallisation gave two compounds; that present in greater amount was *NN'*-di-2-imidazolinylethylenediamine dipicrate, m. p. 253—255°, as proved by its identity with the product from ethylenediamine and 2-methylthioimidazoline [3] or on 2-nitroiminoimidazolidine.[7]



(II) (III)

The second picrate, m. p. 204°, was the dipicrate of *N*-2-imidazolinylethylenediamine, obtained by the action of an excess of ethylenediamine on 2-nitroiminoimidazolidine. 2,3,5,6-Tetrahydro-1*H*-imidaz[1,2*a*]imidazole (III) has been obtained as the monopicrate, m. p. 219—221°, by McKay and his co-workers [8] by a variety of methods; we have confirmed this melting point.

In view of their pharmacological interest a number of 2-aryl(or alkyl)amino-2-oxazolines, some of which show vascular activity,[9] have been prepared by analogous procedures from amino-alcohols. The preparation of guanidinoethanol itself from ethanolamine hydrobromide and cyanamide has been described.[10] 2-Amino-2-oxazolines have also been synthesised by cyclisation of *N*-aryl-*N'*-2-halogenoethylureas [11] in boiling water and by simultaneous dethionation and ring closure of *N*-aryl-*N'*-2-hydroxyethylthioureas (VI) by mercuric oxide in an inert solvent.[12] In the present work some carbodi-imides were caused to react with amino-alcohols.



(IV) (V) (Va) (VI) (VII)

Diphenylcarbodi-imide thus gives exothermally the *NN'*-diphenylguanidinoethanols (IV; R^5 = Ph) in good yield. Heating these in boiling xylene results in elimination of aniline with production of 2-anilino-2-oxazolines (Va; R^5 = Ph) also in good yield. Some new oxazolines have been prepared by this method, but the instability of the dialkylcarbodi-imides and the difficulty of isolation of the products when substituted diphenylcarbodi-imides were used prevented extension of the method.

2-Phenyl(or methyl)amino-2-oxazolines (Va; R^5 = Me or Ph) are also produced in good yield by the action of methyl iodide followed by sodium ethoxide on *N*-2-hydroxyethyl-*N'*-phenyl(or methyl)thioureas (VI; R^5 = Me or Ph) in boiling ethanol. The reaction presumably proceeds through the isothiouronium salt (VII), a route suggested by Goldberg and Kelly [13] who prepared 2-alkyl(and aryl)-2-oxazolines from thioamides by a

[7] McKay, Coleman, and Grant, *J. Amer. Chem. Soc.*, 1950, **72**, 3205.
[8] McKay, Kreling, Paris, Braun, and Whittingham, *Canad. J. Chem.*, 1957, **35**, 843; McKay, Hatton, and Braun, *J. Amer. Chem. Soc.*, 1956, **78**, 6144.
[9] Giudicelli, Beauvallet, Chabrier, and Najer, *Compt. rend.*, 1958, **247**, 891; *ibid.*, p. 2494.
[10] Fromm, Fantle, and Fisch, *J. prakt. Chem.*, 1929, (2), **124**, 167; Schering and Kahlbaum, D.R.P. 462,995; (*a*) Fishbein and Gallaghan, *J. Org. Chem.*, 1956, **21**, 434.
[11] Gabriel and Stelzner, *Ber.*, 1895, **28**, 2929; (*a*) Najer, Chabrier, and Giudicelli, *Bull. Soc. chim. France*, 1959, 532, 1611.
[12] Söderbaum, *Ber.*, 1895, **28**, 1897; Dains, *J. Amer. Chem. Soc.*, 1925, **47**, 1981.
[13] Goldberg and Kelly, *J.*, 1948, 1919.

similar method. In the preparation of 2-anilino-2-oxazoline by this method 1-phenyl-2-imidazolidone was formed as a by-product. Attempts to produce this from phenylurea and ethylenediamine by a published method [14] gave 2-imidazolidone, aniline, and ammonia. A specimen of 1-phenyl-2-imidazolidone was prepared for comparison by the method described by McKay and Braun.[15]

Experimental

2-*Aminoimidazoline*.—(A) Ethylenediamine dihydrochloride (2·7 g., 1 mol.) and *S*-methylisothiouronium sulphate (2·8 g., 1·5 mol.) were dissolved in water (10 ml.), brought to pH 7 with sodium hydrogen carbonate solution, and heated on the steam bath for 2 hr. The residue left after evaporation of the water crystallised from ethanol to give the somewhat hygroscopic 2-*aminoethylguanidinium sulphate*, m. p. 298° (decomp.) (Found: C, 15·4; H, 6·5. $C_3H_{10}N_4,H_2SO_4,2H_2O$ requires C, 15·3; H, 6·8%). The *picrate* had m. p. 246° (Found: C, 32·4; H, 2·7. $C_{15}H_{16}N_{10}O_{14}$ requires C, 32·15; H, 2·9%). The aminoethylguanidinium sulphate (2 g., 1 mol.) was passed in water through Amberlite IRA-400 (OH) resin and evaporated under reduced pressure to a hygroscopic oil from which 2-aminoimidazoline picrate, m. p. 223° (decomp.) (Pierron [1] gave 217°) was obtained as needles from ethanol (Found: C, 34·4; H, 3·3. Calc. for $C_9H_{10}N_6O_7$: C, 34·4; H, 3·2%).

(B) Ethylenediamine monotoluene-*p*-sulphonate (11·6 g., 1 mol.) was heated on the steam bath with cyanamide (4·2 g., 2 mol.) for 3 hr., during which ammonia was given off. The residual syrup was triturated with hot ethanol (30 ml.) and, after cooling, the crystals of *ethylenediguanidinium ditoluene*-p-*sulphonate* (5·5 g.), m. p. 292°, were collected (Found: C, 44·8; H, 6·0. $C_{18}H_{28}N_6O_6S_2$ requires C, 44·3; H, 5·7%). The free *base*, hygroscopic prisms from ethanol–ether, had m. p. 165° (Found: C, 31·3; H, 8·4; N, 55·0. Calc. for $C_4H_{12}N_6,\frac{1}{2}H_2O$: C, 31·4; H, 8·5; N, 54·9%); (lit.,[16] m. p. 163°). The *hydrochloride*, prismatic needles from ethanol–ether, had m. p. 228° (Found: C, 22·5; H, 6·6. $C_4H_{12}N_6,2HCl$ requires C, 22·1; H, 6·5%). The mother liquors from the above toluenesulphonate gave, on evaporation, 2-*aminoimidazoline toluene*-p-*sulphonate*, prismatic needles (from ethanol) (2·6 g., 20%), m. p. 195° (Found: C, 46·6; H, 6·1. $C_{10}H_{15}N_3O_3S$ requires C, 46·7; H, 5·8%). The free base, a syrup, was obtained by treatment of the toluene-*p*-sulphonate with Amberlite IRA-400 and converted into the hygroscopic hydrochloride, needles (from ethanol–ethyl acetate), m. p. 140° (Pierron [1] reports 120—122°) (Found: C, 29·6; H, 6·9; N, 35·0. Calc. for $C_3H_7N_3,HCl$: C, 29·6; H, 6·6; N, 34·5%). The picrate, needles from aqueous ethanol, had m. p. 223° (decomp.) (Pierron [1] gives 217°) (Found: C, 34·4; H, 3·3. Calc. for $C_9H_{10}N_6O_7$: C, 34·4; H, 3·2%). The sulphate, hydrobromide, and nitrate had m. p.s as reported.

(C) Ethylenediamine monotoluene-*p*-sulphonate (5·8 g., 1 mol.) and dimethylcyanamide (1·8 g., 1 mol.) were heated over an open flame for a few seconds to induce the exothermic reaction, which took place with the evolution of dimethylamine. After further heating on the steam bath for 3 hr., the semicrystalline mass was dissolved in hot ethanol and allowed to crystallise (yield: 3·0 g., 46%; m. p. 195°).

2-*Amino*-1,4,5,6-*tetrahydropyrimidine*.—(A) Trimethylenediamine ditoluene-*p*-sulphonate (10·45 g., 1 mol.), the free diamine (1·85 g., 1 mol.), and dimethylcyanamide (3·5 g., 2 mol.) were heated over a free flame until an exothermic reaction took place, and then on the water bath for 10 min. Crystallisation from ethanol gave 2-*amino*-1,4,5,6-*tetrahydropyrimidine monotoluene*-p-*sulphonate* (7 g., 52%), m. p. 175° (Found: C, 48·5; H, 6·2. $C_{11}H_{17}N_3O_3S$ requires C, 48·7; H, 6·3). The picrate (from ethanol) had m. p. 184° (Found: C, 36·5; H, 3·8. Calc. for $C_{10}H_{12}N_6O_7$: C, 36·6; H, 3·6%) (lit.,[10a] m. p. 188—200°).

(B) Trimethylenediamine ditoluene-*p*-sulphonate (3 g., 1 mol.), the free diamine (0·53 g., 1 mol.), and cyanamide (0·9 g., 1·5 mol.) were heated on the water bath for 45 min. The solid residue crystallised from ethanol to give 2-amino-1,4,5,6-tetrahydropyrimidine monotoluene-*p*-sulphonate, m. p. 175° (2·3 g., 59%). The mother liquors contained trimethylenediguanidine which was precipitated as the dipicrate,[18] m. p. 242° (1 g., 1·1%) (Found: C, 32·9; H, 3·15. Calc. for $C_{17}H_{20}N_{12}O_{14}$: C, 33·2; H, 3·2%).

[14] U.S.P. 2,517,750.
[15] McKay and Braun, *J. Org. Chem.*, 1951, **16**, 1829.
[16] Jap. P. 154,050.
[17] Stefanye and Howard, *J. Amer. Chem. Soc.*, 1955, **77**, 761.
[18] Schenck and Kirchhof, *Z. physiol. Chem.*, 1926, **158**, 107.

2-Amino-4-methylimidazoline.—(*A*) Propylenediamine monotoluene-*p*-sulphonate (12·3 g., (1 mol.) was heated gently over a free flame with dimethylcyanamide (3·5 g., 1 mol.) until an exothermic reaction took place, and then for a further 2·5 hr. on the water bath. Crystallisation from ethanol–ether gave *2-amino-4-methylimidazoline monotoluene*-p-*sulphonate* (6·2 g., 46%) as needles, m. p. 135° (Found: C, 48·8; H, 6·5. $C_{11}H_{17}N_3O_3S$ requires C, 48·7; H, 6·3%). The *nitrate*, colourless leaflets from ethanol–ether, had m. p. 87° (Found: C, 29·6; H, 6·0. $C_4H_{10}N_4O_3$ requires C, 29·6; H, 6·2%), and the *picrate*, needles from aqueous ethanol, had m. p. 195° (Found: C, 37·0; H, 3·9. $C_{10}H_{12}N_6O_7$ requires C, 36·6; H, 3·7%).

(*B*) Propylenediamine monotoluene-*p*-sulphonate (1 mol.) and cyanamide (1 mol.) were heated on the water bath for 3 hr. Crystallisation from ethanol gave a small yield of 2-amino-4-methylimidazoline monotoluene-*p*-sulphonate.

2-Anilino-4-methylimidazoline.—Propylenediamine monotoluene-*p*-sulphonate (6·15 g., 1 mol.) and phenylcyanamide (5·9 g., 2 mol.) were heated together on the water bath for 3 hr. The oily residue was converted into *2-anilino-4-methylimidazoline picrate*, m. p. 148° (Found: C, 47·8; H, 4·1. $C_{16}H_{16}N_6O_7$ requires C, 47·5; H, 4·0%). The picrate in aqueous ethanol was passed through a column of IRA-400 (OH^-) resin. Evaporation of the eluate under reduced pressure gave 2-anilino-4-methylimidazoline, colourless needles (from benzene), m. p. 81° (Found: C, 68·4; H, 7·5. $C_{10}H_{13}N_3$ requires C, 68·6; H, 7·4%).

2-Anilino-1,4,5,6-tetrahydropyrimidine.—Trimethylenediamine ditoluene-*p*-sulphonate (10·45 g., 1 mol.), the free diamine (1·85 g., 1 mol.), and phenylcyanamide (5·9 g., 2 mol.) were heated over a free flame until an exothermic reaction set in and then for 2 hr. on the water bath. The residue was crystallised from ethanol to give *2-anilino-1,4,5,6-tetrahydropyrimidine monotoluene*-p-*sulphonate* as prismatic needles, m. p. 167° (5 g., 29%) (Found: C, 58·8; H, 5·8. $C_{17}H_{21}N_3O_2S$ requires C, 58·9; H, 6·1%). The *picrate* (from aqueous ethanol) had m. p. 200° (Found: C, 47·8; H, 4·0. $C_{16}H_{16}N_6O_7$ requires C, 47·5; H, 4·0%).

2-Amino-3a,4,5,6,7,7a-hexahydrobenzimidazole.—*Cyclohexane-1,2-diamine monotoluene*-p-*sulphonate* (7·2 g., 1 mol.), prepared by crystallising equimolecular amounts of the diamine and the acid from ethanol (m. p. 181°) (Found: C, 54·2; H, 7·5. $C_{13}H_{22}O_3N_2S$ requires C, 54·5; H, 7·7%), and dimethylcyanamide (3·5 g., 2 mol.) were heated together over the open flame to start the reaction, then further heated for 3 hr. on the steam bath. The product, crystallised from ethanol–ether, gave the *2-aminohexahydrobenzimidazole toluene*-p-*sulphonate* (1·2 g.), m. p. 233° (Found: C, 54·2; H, 7·0. $C_{14}H_{21}N_3O_3S$ requires C, 54·0; H, 6·8%). The *picrate*, needles from aqueous ethanol, had m. p. 188° (Found: C, 42·1; H, 4·7. $C_{13}H_{16}N_6O_7$ requires C, 42·4; H, 4·4%). The *nitrate*, prisms from ethanol, had m. p. 201° (Found: C, 41·4; H, 7·0. $C_7H_{13}N_3,HNO_3$ requires C, 41·6; H, 6·9%). The free *base*, needles from ethanol, had m. p. 174° (Found: C, 60·2; H, 9·2. $C_7H_{13}N_3$ requires C, 60·4; H, 9·4%).

2-Aminobenzimidazole.—*o*-Phenylenediamine monotoluene-*p*-sulphonate (9·2 g., 1 mol.) was heated with cyanamide (1·4 g., 1 mol.) at 180° for 8 hr., evolution of ammonia then having ceased. Crystallisation from ethanol gave *2-aminobenzimidazole toluene*-p-*sulphonate* (4·6 g., 46%), prisms, m. p. 190·5—191·5° (Found: C, 54·9; H, 4·7; N, 14·15; S, 10·8. $C_{14}H_{15}N_3SO_3$ requires C, 55·0; H, 4·9; N, 13·8; S, 10·5%). Crystallisation from benzene–light petroleum (b. p. 60—80°) gave 2-aminobenzimidazole as plates, m. p. and mixed m. p. 222°.

2-Dimethylaminobenzimidazole.—(*A*) *o*-Phenylenediamine monotoluene-*p*-sulphonate (12 g., 1 mol.) was heated at 160° for 24 hr. with dimethylcyanamide (3 g., 1 mol.); evolution of basic fumes had then ceased. The residue was crystallised repeatedly from ethanol to give *2-dimethylaminobenzimidazole monotoluene*-p-*sulphonate*, needles, m. p. 256—257° (decomp.) (1·75 g., 12%) (Found: C, 57·45; H, 5·7; N, 12·5. $C_{16}H_{19}N_3SO_3$ requires C, 57·7; H, 5·8; N, 12·6%). The salt was triturated with sodium hydroxide solution and filtered. Crystallisation from ethanol gave 2-dimethylaminobenzimidazole as needles, m. p. 312—313° (Found: C, 67·4; H, 6·7. Calc. for $C_9H_{11}N_3$: C, 67·1; H, 6·8%).

(*B*) 2-Chlorobenzimidazole (1·5 g., 1 mol.) was heated with dimethylamine hydrochloride (0·9 g., 1·1 mol.), potassium hydroxide (1·2 g., 2·1 mol.), and water (8 ml.) at 155—160° for 6 hr. The crystalline product, recrystallised from ethanol, gave 2-dimethylaminobenzimidazole, needles, m. p. 312—314° (1·4 g., 87%).

2-Anilinoimidazoline.—(*A*) Ethylenediamine monotoluene-*p*-sulphonate (5 g., 1 mol.) and phenylcyanamide (5 g., 2 mol.) were heated on the steam bath for 3 hr., after which ammonia ceased to be evolved. The semi-solid mass of impure toluenesulphonate (1·4 g.) was dissolved in hot alcohol and allowed to crystallise. Treatment of this material with aqueous picric acid

gave 2-*anilinoimidazoline picrate*, m. p. 193°, needles from ethanol (Found: C, 46·4; H, 3·9. $C_{15}H_{14}N_6O_7$ requires C, 46·2; H, 3·6%). A solution of the picrate in aqueous ethanol, passed through Amberlite IRA-400, gave on evaporation the free base, m. p. 135° (lit.,[19] m. p. 136°), plates from ethanol (Found: C, 66·8; H, 6·9. Calc. for $C_9H_{11}N_3$: C, 67·1; H, 6·8%); this gave the *hydrochloride*, m. p. 212°, plates from ethanol (Found: C, 55·0; H, 6·3. $C_9H_{11}N_3$,HCl requires C, 54·7; H, 6·1%). From the above impure toluenesulphonate it was possible to obtain by fractional crystallisation a small quantity of *ethylenedi*-(N-*phenylguanidine*), m. p. 183°, prismatic needles from ethanol (Found: C, 64·9; H, 6·9. $C_{16}H_{20}N_6$ requires C, 64·9; H, 6·8%) [*dihydrochloride*, m. p. 230°, needles from aqueous ethanol (Found: C, 51·6; H, 6·2; N, 22·6. $C_{16}H_{20}N_6$,2HCl requires C, 52·0; H, 6·0; N, 22·8%)].

(*B*) 2-Methylthioimidazoline hydriodide (2·4 g., 1 mol.) and aniline (2·8 g., 3 mol.) were heated at 130° for 3 hr.; then methanethiol ceased to be evolved. Ethanol was then added and the sparingly soluble crystalline material, which did not give a picrate, was removed. The picrate, m. p. 193°, prepared from the filtrate, was passed in solution through the ion-exchange resin to give the free base, m. p. 135°, identical with the product prepared as above.

(*C*) Ethylenediamine monotoluene-*p*-sulphonate (5 g., 1 mol.) was boiled in ethanol (100 ml.) with diphenylcarbodi-imide (4·175 g., 1 mol.) for 4 hr. The solvent and aniline were removed *in vacuo* and the oily residue crystallised from ethanol–ether, to give 2-*anilinoimidazoline monotoluene*-p-*sulphonate* (6·2 g., 86%), needles, m. p. 133—134° (Found: C, 57·6; H, 5·9. $C_{16}H_{19}N_3O_3S$ requires C, 57·7; H, 5·7%). The picrate had m. p. 195°, alone or mixed with the specimen from the previous preparation. The free base was prepared from the toluene-sulphonate by treatment with Amberlite IRA-400 (OH^-) resin.

NN′-*Di*-2-*imidazolinylethylenediamine*.—This was produced as the dipicrate by the methods described by McKay *et al.*[7] and Aspinall and Bianco;[3] it had m. p. 254—255° (lit., m. p. 268—269,[7] 259—261°[3]) (Found: C, 36·6; H, 3·5; N, 25·3. Calc. for $C_{20}H_{22}N_{12}O_{14}$: C, 36·75; H, 3·4; N, 25·6%).

N-2-*Imidazolinylethylenediamine*.—The dipicrate, made as described by McKay *et al.*,[7] had m. p. 204° (lit., m. p. 205—206·5°) (Found: C, 35·0; H, 3·4; N, 24·25. Calc. for $C_{17}H_{18}N_{10}O_{14}$: C, 34·9; H, 3·1; N, 23·9%).

2-Amino-2-imidazoline hydrobromide (1·9 g., 1 mol.) in water was mixed with ethylenediamine (0·7 g., 1 mol.) and heated at 100° for 48 hr. Further ethylenediamine (1·4 g., 2 mol.) was added during the first 40 hr. After being heated finally at 130—150° for 2 hr. to remove the excess of ethylenediamine, the residue was converted into the picrate. Crystallisation from ethanol gave a small yield of *N*-2-imidazolinylethylenediamine dipicrate, m. p. 204°. The ethanol-insoluble material crystallised from aqueous ethanol to give *NN′*-di-2-imidazolinylethylenediamine dipicrate, m. p. 253—255°.

N-2-*Hydroxyethyl*-N′-*phenylthiourea*.—Phenylisothiocyanate (20 g., 1 mol.) was slowly added to a solution of ethanolamine (9·04 g., 1 mol.) in benzene (100 ml.). An exothermic reaction took place and the mixture was left at room temperature for 2 hr. The product crystallised from ethanol as needles, m. p. 139° (Knorr and Rossler[20] report 138°) (28 g., 96·5%).

New *thioureas* prepared in this way were: N-(2-*hydroxy*-1-*phenylethyl*)-N′-*phenyl*- (VI; $R^1 = R^5 = Ph$, $R^2 = R^3 = H$), m. p. 164°, needles from ethanol, in 91% yield (Found: C, 66·2; H, 5·8. $C_{15}H_{16}N_2OS$ requires C, 66·1; H, 5·9%); N-2-*hydroxyethyl*-N′-*methyl*- (VI; R's = H, except $R^5 = Me$), m. p. 73°, prisms from chloroform–light petroleum, in 70% yield (Found: C, 35·7; H, 7·7. $C_4H_{10}N_2OS$ requires C, 35·9; H, 7·45%); *N*-(2-hydroxy-1,1-dimethylethyl)-*N*′-phenyl- (VI; $R^1 = R^2 = Me$, $R^3 = H$, $R^5 = Ph$), m. p. 131° (lit.,[21] 127—128·5°) (Found: C, 59·0; H, 7·4. Calc. for $C_{11}H_{16}N_2OS$; C, 59·0; H, 7·15%).

2-*Imidazolidone*.—Phenylurea (10 g., 1 mol.) was heated with ethylenediamine hydrate (20 g., 3·5 mol.) in toluene (150 ml.) at 100° for 4 hr. The temperature was raised to 140° for 2 hr. and the excess of diamine distilled off together with the solvent and some ammonia. Heating at 150—160°/15 mm. removed aniline, and the residue solidified. Crystallisation from chloroform gave 2-imidazolidone, colourless prisms (4 g., 63%), m. p. 132° (lit.,[22] 131°), and not 1-phenyl-2-imidazolidone as claimed earlier.[14]

[19] G.P. 842,065.
[20] Knorr and Rossler, *Ber.*, 1903, **36**, 1280.
[21] VanderWerf, Heisler, and McEwen, *J. Amer. Chem. Soc.*, 1954, **76**, 1231.
[22] Tafel and Reindl, *Ber.*, 1901, **34**, 3288.

N-2-*Hydroxyethyl*-N'N''-*diphenylguanidine* (IV; R's = H except R^5 = Ph).—Ethanol amine (1 g., 1 mol.) in benzene (10 ml.) was added to diphenylcarbodi-imide (3·2 g., 1 mol.) in benzene (10 ml.). An exothermic reaction took place. After 1 hr. the solvent was removed *in vacuo* and the residue crystallised from chloroform–light petroleum (b. p. 40—60°) to give the *guanidine*, needles, m. p. 109—110° (3·9 g., 93%) (Found: C, 70·4; H, 6·5. $C_{15}H_{17}N_3O$ requires C, 70·6; H, 6·6%).

Also prepared by this method were N-2-*hydroxypropyl*-N'N''-*diphenyl*-, needles, m. p. 157° [from chloroform–light petroleum (b. p. 40—60°); 60% yield] (Found: C, 71·2; H, 7·1; N, 15·45. $C_{16}H_{19}N_3O$ requires C, 71·4; H, 7·1; N, 15·6%), and N'-2-*hydroxyethyl*-N-*methyl*-N''-*diphenyl-guanidine*, needles, m. p. 129—130° [from benzene–light petroleum (b. p. 40—60°); 69% yield] (Found: C, 71·1; H, 7·2; N, 15·7. $C_{16}H_{19}N_3O$ requires C, 71·4; H, 7·1; N, 15·6%).

Other guanidino-compounds prepared were cyclised directly without isolation.

2-*Anilino*-2-*oxazoline*.—(*A*) *N*-2-Hydroxyethyl-*N'N''*-diphenylguanidine (1·95 g.) was refluxed in xylene for 0·5 hr., and the solvent removed together with aniline. Crystallisation from chloroform–light petroleum (b. p. 40—60°) gave 2-anilino-2-oxazoline,[11] colourless needles, m. p. 119—120° (1·14 g., 92%) (Found: C, 66·9; H, 6·2; N, 17·1. Calc. for $C_9H_{10}N_2O$: C, 66·7; H, 6·2; N, 17·3%). The picrate had m. p. 187° (decomp.) (lit.,[11] 175°) (Found: C, 45·8; H, 3·3. Calc. for $C_{15}H_{13}N_5O_8$: C, 46·0; H, 3·3%).

(*B*) *N*-2-Hydroxyethyl-*N'*-phenylthiourea (7 g., 1 mol.) in ethanol (70 ml.) was refluxed with methyl iodide (7·6 g., 1·5 mol.) for 1 hr. Sodium ethoxide [from sodium (2·05 g., 2·5 mol.) in ethanol (80 ml.)] was added and the mixture refluxed (further 3 hr.) until evolution of methanethiol ceased. The solvent was removed *in vacuo* and water (100 ml.) added. After cooling to 5°, the colourless solid was collected and washed with ice-water. Crystallisation as above gave 2-anilino-2-oxazoline (3·9 g., 67%). The alkaline mother liquors were extracted

2-(Substituted amino)-2-oxazolidines (V) and -oxazolines (Va) and their derivatives.

						Yield [g]		Found (%)				Required (%)		
R^1	R^2	R^3	R^4	R^5	Method	(%)	M. p.	C	H	N	Formula	C	H	N
H	H	H	H	Ph	A	86 [a]	119—120° [h]	66·9	6·2	17·1	$C_9H_{10}N_2O$	66·7	6·2	17·3
					B	67								
	Picrate [b]						187 [i]	45·8	3·3	—	$C_{15}H_{13}N_5O_8$	46·0	3·3	—
H	H	H	H	Me	B	40 [a]	106—108	47·7	8·2	28·4	$C_4H_8N_2O$	48·0	8·0	28·0
	Picrate [c]						165—166 [p]	36·6	3·55	—	$C_{10}H_{11}N_5O_8$	36·5	3·35	—
Et	H	H	H	Ph	A	61 [d]	100—101 [j]	69·3	7·6	14·6	$C_{11}H_{14}N_2O$	69·5	7·4	14·7
					B	50								
	Picrate [e]						135	48·7	4·2	—	$C_{17}H_{17}N_5O_8$	48·7	4·1	—
Ph	H	H	H	Ph	A	69 [d]	156—157	75·4	5·9	11·75	$C_{15}H_{14}N_2O$	75·6	5·9	11·8
					B	80								
	Picrate [b]						196	53·8	3·6	—	$C_{21}H_{17}N_5O_8$	54·0	3·6	—
H	H	Me	H	Ph	A	55 [a]	134 [km]	68·2	6·7	15·8	$C_{10}H_{12}N_2O$	68·2	6·8	15·9
					B	82								
	Picrate						169 [n]	47·5	3·8	—	$C_{16}H_{15}N_5O_8$	47·5	3·7	—
Me	Me	H	H	Ph	A	70	114—116	69·4	7·3	14·9	$C_{11}H_{14}N_2O$	69·5	7·4	14·7
					B	85								
	Picrate [b]						205	48·5	4·2	—	$C_{17}H_{17}N_5O_8$	48·7	4·1	—
H	H	H	Me	Ph	A	65 [d]	82	68·4	6·55	15·7	$C_{10}H_{12}N_2O$	68·2	6·8	15·9
	Hydrochloride [g]						111	56·5	6·05	—	$C_{10}H_{13}ClN_2O$	56·5	6·1	—
Me	H	Ph	H	Ph	A	71 [a]	140	76·0	6·3	11·5	$C_{16}H_{16}N_2O$	76·2	6·3	11·1
	Hydrochloride [g]						156	66·3	6·5	9·9	$C_{16}H_{17}ClN_2O$	66·4	6·7	9·7
Me	H	Ph	Me	Ph	A									
	Hydrochloride [g]					84	187	67·5	6·4	—	$C_{17}H_{19}ClN_2O$	67·3	6·3	—

Crystallised from (*a*) chloroform–light petroleum (b. p. 40—60°), (*b*) aqueous ethanol, (*c*) water, (*d*) benzene–light petroleum, (*e*) ethanol, (*f*) ether–light petroleum, (*g*) ethanol–ether.

Recorded m. p.: (*h*) [11] 119—120°; (*i*) [11] 175°; (*j*) [11a] 102°; (*k*) [11a] 141°; (*m*) [23] 132°; (*n*) [23] 166—168°; (*p*) [24] 167°.

(*q*) Yields by method A are overall based on the amino-alcohol.

The optically active amino-alcohols were the (±)-forms except that (−)-ephedrine was used for the preparation of 3,4-dimethyl-5-phenyl-2-phenylimino-oxazolidine. β-Aminophenethyl alcohol was prepared from styrene oxide and sodium azide.[25]

[23] Meene, *Ber.*, 1900, **33**, 657.
[24] McKay, *Canad. J. Chem.*, 1953, **31**, 284.
[25] McEwen, Conrad, and VanderWerf, *J. Amer. Chem. Soc.*, 1952, **74**, 1168.

with chloroform (5 × 80 ml.). The colourless residue left on evaporation was washed with dilute hydrochloric acid (20 ml.) and then with water. Crystallisation from chloroform–light petroleum gave 1-phenyl-2-imidazolidone, needles (0·1 g., 1·7%), m. p. 162—163°, not depressed by a specimen prepared by the method of McKay and Braun [15] (Found: C, 66·6; H, 6·0; 17·3. Calc. for $C_9H_{10}N_2O$: C, 66·7; H, 6·2; N, 17·3%).

The Table lists the oxazolidines and oxazolines produced by these methods.

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